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Childhood cancer and nuclear power plants in Switzerland: a census-based cohort study

Spycher, B D ; Feller, M ; Zwahlen, M ; Rösli, M ; von der Weid, N X ; Hengartner, H ; Egger, M ; Kuehni, C E

Abstract: **BACKGROUND:** Previous studies on childhood cancer and nuclear power plants (NPPs) produced conflicting results. We used a cohort approach to examine whether residence near NPPs was associated with leukaemia or any childhood cancer in Switzerland. **METHODS:** We computed person-years at risk for children aged 0-15 years born in Switzerland from 1985 to 2009, based on the Swiss censuses 1990 and 2000 and identified cancer cases from the Swiss Childhood Cancer Registry. We geo-coded place of residence at birth and calculated incidence rate ratios (IRRs) with 95% confidence intervals (CIs) comparing the risk of cancer in children born <5 km, 5-10 km and 10-15 km from the nearest NPP with children born >15 km away, using Poisson regression models. **RESULTS:** We included 2925 children diagnosed with cancer during 21 117 524 person-years of follow-up; 953 (32.6%) had leukaemia. Eight and 12 children diagnosed with leukaemia at ages 0-4 and 0-15 years, and 18 and 31 children diagnosed with any cancer were born <5 km from a NPP. Compared with children born >15 km away, the IRRs (95% CI) for leukaemia in 0-4 and 0-15 year olds were 1.20 (0.60-2.41) and 1.05 (0.60-1.86), respectively. For any cancer, corresponding IRRs were 0.97 (0.61-1.54) and 0.89 (0.63-1.27). There was no evidence of a dose-response relationship with distance ($P > 0.30$). Results were similar for residence at diagnosis and at birth, and when adjusted for potential confounders. Results from sensitivity analyses were consistent with main results. **CONCLUSIONS:** This nationwide cohort study found little evidence of an association between residence near NPPs and the risk of leukaemia or any childhood cancer.

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Childhood cancer and nuclear power plants in Switzerland: a census-based cohort study

Ben D Spycher,^{1,2†} Martin Feller,^{1†} Marcel Zwahlen,¹ Martin Röösl, ^{3,4} Nicolas X von der Weid,⁵ Heinz Hengartner,⁶ Matthias Egger,^{1,2} Claudia E Kuehni,^{1*} for the Swiss Paediatric Oncology Group[‡] and the Swiss National Cohort Study Group[‡]

¹Division of International and Environmental Health, Institute of Social and Preventive Medicine (ISPM), University of Bern, Bern, Switzerland, ²School of Social and Community Medicine, University of Bristol, Bristol, UK, ³Swiss Tropical and Public Health Institute, Basel, Switzerland, ⁴University of Basel, Switzerland, ⁵Paediatric Haematology-Oncology Unit, Centre Hospitalier Universitaire Vaudois, Service de Pédiatrie, Lausanne-CHUV, Switzerland and ⁶Ostschweizer Kinderspital, St Gallen, Switzerland

*Corresponding author. Division of International and Environmental Health, Institute of Social and Preventive Medicine (ISPM), Finkenhubelweg 11, CH-3012 Bern, Switzerland. E-mail: kuehni@ispm.unibe.ch

†These authors contributed equally to this work.

‡See Acknowledgements for a list of the members of the Swiss Paediatric Oncology Group and the Swiss National Cohort Study Group.

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Background Previous studies on childhood cancer and nuclear power plants (NPPs) produced conflicting results. We used a cohort approach to examine whether residence near NPPs was associated with leukaemia or any childhood cancer in Switzerland.

Methods We computed person-years at risk for children aged 0–15 years born in Switzerland from 1985 to 2009, based on the Swiss censuses 1990 and 2000 and identified cancer cases from the Swiss Childhood Cancer Registry. We geo-coded place of residence at birth and calculated incidence rate ratios (IRRs) with 95% confidence intervals (CIs) comparing the risk of cancer in children born <5 km, 5–10 km and 10–15 km from the nearest NPP with children born >15 km away, using Poisson regression models.

Results We included 2925 children diagnosed with cancer during 21 117 524 person-years of follow-up; 953 (32.6%) had leukaemia. Eight and 12 children diagnosed with leukaemia at ages 0–4 and 0–15 years, and 18 and 31 children diagnosed with any cancer were born <5 km from a NPP. Compared with children born >15 km away, the IRRs (95% CI) for leukaemia in 0–4 and 0–15 year olds were 1.20 (0.60–2.41) and 1.05 (0.60–1.86), respectively. For any cancer, corresponding IRRs were 0.97 (0.61–1.54) and 0.89 (0.63–1.27). There was no evidence of a dose-response relationship with distance ($P > 0.30$). Results were similar for residence at diagnosis and at birth, and when adjusted for potential confounders. Results from sensitivity analyses were consistent with main results.

Conclusions This nationwide cohort study found little evidence of an association between residence near NPPs and the risk of leukaemia or any childhood cancer.

Keywords Childhood, cancer, leukaemia, ionizing radiation, nuclear power plants, population based, cancer registry

Introduction

Since Black reported a cluster of children with leukaemia near Sellafield in 1984,¹ numerous studies investigated cancer incidence near nuclear power plants (NPP), with conflicting results. Some found an increased risk also at places where NPPs were planned but not built, concluding that factors other than radiation might be responsible.^{2,3} A recent case-control study from Germany, which reported odds ratios (ORs) of 1.61 for all cancers and 2.19 for leukaemia in 0–4 year olds living <5 km from a NPP, refuelled the debate on a possible link between NPPs and childhood cancer.^{4,5}

Most previous analyses were ecological and may have been affected by exposure misclassification and confounding.^{6–11} The German case-control study was criticized for potential selection and participation bias.^{4,5,12,13} A recent Finnish study combining ecological, cohort and case-control analyses was small, with no children living <5 km from NPPs.¹⁴ All previous studies analysed residence at diagnosis. Given the higher vulnerability to radiation of fetuses and infants and the latency between radiation exposure and cancer development, residence at birth might be more relevant.¹⁵

We investigated the risk of childhood leukaemia and all childhood cancers in the vicinity of Swiss NPPs, using a cohort approach with person-years derived from the Swiss censuses 1990 and 2000 and incident cases from the Swiss Childhood Cancer Registry (SCCR). We analysed distance of residence at birth to the nearest NPP in the main analysis, and distance to residence at diagnosis in a secondary analysis. Outcomes of interest were leukaemia and all cancers diagnosed at ages 0–4 (<5) and 0–15 (<16) years. We adjusted for confounders, included other nuclear installations (research reactors and storage sites), and locations where NPPs were planned but not built, and assessed the robustness of the results in sensitivity analyses.

Methods

Nuclear facilities in Switzerland

Figure 1 shows the location of Switzerland's five NPPs: Beznau I and II (in operation since 1969 and 1971), Leibstadt (6 km from Beznau, since 1984), Mühleberg (since 1972) and Gösgen (since 1979). Other nuclear facilities include three research reactors (Universities of Lausanne and Basel and Paul Scherrer Institute [PSI] in Villigen, operating since 1983, 1959 and 1957, respectively), a prototype reactor (Lucens, 1968–69, shut down after a partial meltdown) and an interim storage facility in Würenlingen (since 2001). Airborne and liquid radioactive discharges and direct radiation in the vicinity of facilities are monitored.¹⁶ Emissions are comparable to those reported from France, Germany and the UK.¹³ In 2009, the total exposure to ionizing radiation of the Swiss population

was estimated at 5.5 mSv/year, including 3.2 mSv from radon, 1.2 mSv from medical and 0.75 mSv from cosmic and terrestrial radiation.¹⁶ Among people living in the vicinity of a NPP, a small fraction of the annual exposure (<0.01 mSv/year) was attributable to discharges from the NPP. At five sites (Graben, Inwil, Kaiseraugst, Rüthi, Verbois), NPPs had been planned but not built.

Definition of birth and resident cohorts

We analysed two cohorts: a birth cohort and a resident cohort. For both cohorts, person-time at risk was calculated based on the censuses 1990 and 2000 using data from the Swiss National Cohort.¹⁷ The birth cohort included all children born in Switzerland between January 1985 and December 2009 and person-time at risk was measured from birth. The resident cohort included all 0–15 year olds residing in Switzerland for any amount of time between January 1985 and December 2009. Person-time at risk was measured from the date the child entered the cohort.

All children diagnosed with cancer 1985–2009 and registered in the population-based Swiss Childhood Cancer Registry (SCCR, www.childhoodcancerregistry.ch)^{18,19} were eligible. The SCCR includes all children diagnosed with leukaemia, malignant solid tumours or brain tumours classified according to the International Classification of Childhood Cancer (ICCC3).²⁰ Children with Langerhans cell histiocytosis are also included. Completeness of registration is >90% and incidence rates are similar to other countries with national registries.^{18,19,21}

Exposure assessment and geo-coding

Study exposures were the distance of the residence from the nearest nuclear facility at birth (birth cohort, main analysis) or the distance at diagnosis (resident cohort, secondary analysis). We considered (i) distance to the nearest NPP, (ii) smallest distance to any nuclear facility and (iii) distance to nearest planned but not built NPP. Address at diagnosis is collected routinely in the SCCR. For this study, we additionally obtained resident histories back to birth by contacting the communal population registries. Addresses of cancer cases were geo-coded by the Swiss Federal Statistical Office (FSO) using specialized software, or coded manually using the fixpoint data service (FPDS) of the Swiss Federal Office of Topography (<http://map.fdds.admin.ch>). The census data include geo-codes of almost all residents. Distances were computed using ArcGIS (ArcGIS 9.3; Redlands, CA, USA).

Potential confounders

Informed by the literature,²² we considered the following potential confounders: (i) background ionizing radiation (cosmic, terrestrial, artificial and total radiation); (ii) electromagnetic radiation from radio and

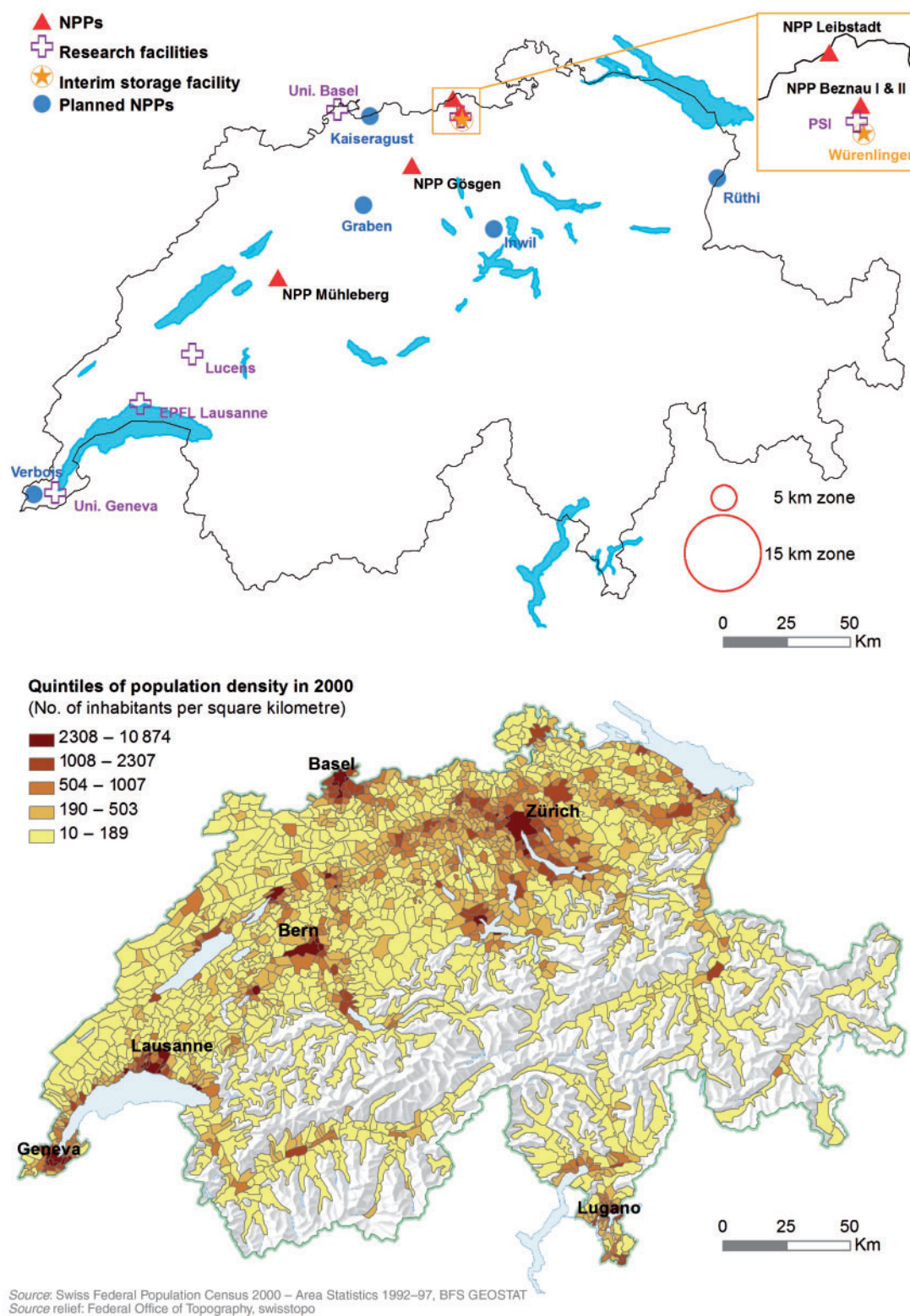


Figure 1 Maps showing sites of nuclear facilities and population density in Switzerland. Locations of NPPs, research facilities, the interim storage facility and sites where NPPs were planned but never built (upper map) and population density in 2000 in quintiles (lower map)
NPP, nuclear power plant; EPFL, École Polytechnique Fédérale de Lausanne; Uni, University; PSI, Paul Scherrer Institute

TV transmitters (from an area exposure model), multi-track railways and high voltage (≥ 200 kV) power lines (indexed by distance to nearest installation); (iii) carcinogens related to traffic exhaust (distance to major roads); (iv) agricultural pesticides (distance to the nearest land use plot with fruit trees, vineyards and golf courses); (v) socio-economic status measured at community level based on income, education and job position (Sotomo Index);²³ (vi) population mixing and exposure to childhood infections (indexed by average number of children per household in the community and degree of urbanization). We also adjusted for distance to the nearest paediatric cancer centre, which may have affected the probability of registration in the SCCR. Details on data sources and variable definitions are given in [Supplementary Appendix 1](#), available as [Supplementary Data](#) at *IJE* online.

Statistical analysis

We used Poisson regression to estimate incidence rate ratios (IRRs) and 95% CIs, comparing children living <5 km, 5–10 km and 10–15 km from the nearest NPP with those living >15 km away, adjusting for sex, age and calendar year. We calculated the number of cases and person-years at risk attributable to each combination of exposure (four strata), sex, age (five or 16 strata), calendar year (1985–2009, 25 strata) and one potential confounder. Due to small numbers, we only included one confounder at a time. For each cohort, we calculated person-years in 1990 and 2000 using census data and, from these values, person-years before (1985–89), between (1991–99) and after the censuses (2001–09) by linear extra- and interpolation.²⁴ The calculations are described in detail in [Supplementary Appendix 1](#), available as [Supplementary Data](#) at *IJE* online.

We performed 10 additional analyses, including eight sensitivity analyses (the rationale for these analyses is given in Box 1): (1) accounting for main dispersal directions of airborne emissions from NPPs (see [Figure E31](#) in [Supplementary Appendix 2](#), available as [Supplementary Data](#) at *IJE* online); (2) excluding children living >50 km from a NPP; (3) excluding calendar years 1985–90 and 2009, when registration in the SCCR was less complete; (4) excluding children born abroad or before 1985 from the resident cohort; (5) using an alternative method for calculating person-years (see [Supplementary Appendix 1](#), available as [Supplementary Data](#) at *IJE* online); (6) recalculating distance to nearest NPP by excluding each NPP in turn; (7) stratifying by calendar period (1985–94; 1995–2009); (8) including only children who remained in the community where they were born.

Finally, we performed two analyses using distance to nearest NPPs as a continuous rather than a categorical variable (Box 1): (9) we used $1/(\text{distance in km})$ as the exposure measure; (10) we compared distances to nearest NPPs between cases and the

population at risk using two-sample *t*-tests and the Mann–Whitney U-test (see [Supplementary Appendix 2](#), available as [Supplementary Data](#) at *IJE* online). The latter approach is related to the case-specular method in case–control research.²⁵ Stata version 11.0 (StataCorp, College Station, TX, USA) was used for all analyses.

Results

Selection of childhood cancer cases and geo-coding

Geo-coded addresses were available for 2925 children diagnosed in the birth cohort and for 4090 cases in the resident cohort (Figure 2). Precision was <50 m for 95% of geo-codes. Among cases in the birth cohort, 1976 (67.6%) had not moved between birth and diagnosis, 648 (22.2%) had moved once, 191 (6.5%) twice and 110 (3.8%) three times or more. Of the 1 240 198 and 1 333 538 children aged 0–15 years registered in the censuses 1990 and 2000, 1 191 536 (96.1%) and 1 301 465 (97.6%), respectively, had geo-coded addresses.

Characteristics of childhood cancer cases

Among the 2925 cancer cases in the birth cohort, 953 (32.6%) had been diagnosed with leukaemia, 303 (10.4%) with lymphoma and 594 (20.3%) with a neoplasm of the central nervous system (Table 1). The distribution of diagnoses was similar in the 4090 children included in the resident cohort, and comparable to the SCCR in general.^{18,19} The 1250 and 85 children excluded from birth and resident cohorts, respectively, had higher proportions of lymphomas and bone tumours as they were, on average, older at diagnosis (Table 1).

Incidence of childhood cancer in birth and resident cohorts

Observation time in the birth cohort totalled 21 117 524 person-years. The incidence per 100 000 person-years in children aged 0–15 years was 4.51 (95% CI 4.24–4.81) for leukaemia and 13.85 (13.36–14.36) for all cancers. The corresponding figures for the resident cohort were 31 279 898 person-years at risk, 4.30 (95% CI 4.08–4.54) and 13.08 (95% CI 12.68–13.48) per 100 000 person-years. [Table E1](#) in [Supplementary Appendix 2](#) presents incidence rates for leukaemia and all cancers by sex, age and calendar year. Incidence was higher in boys than in girls, higher in younger children and slightly higher in recent years.

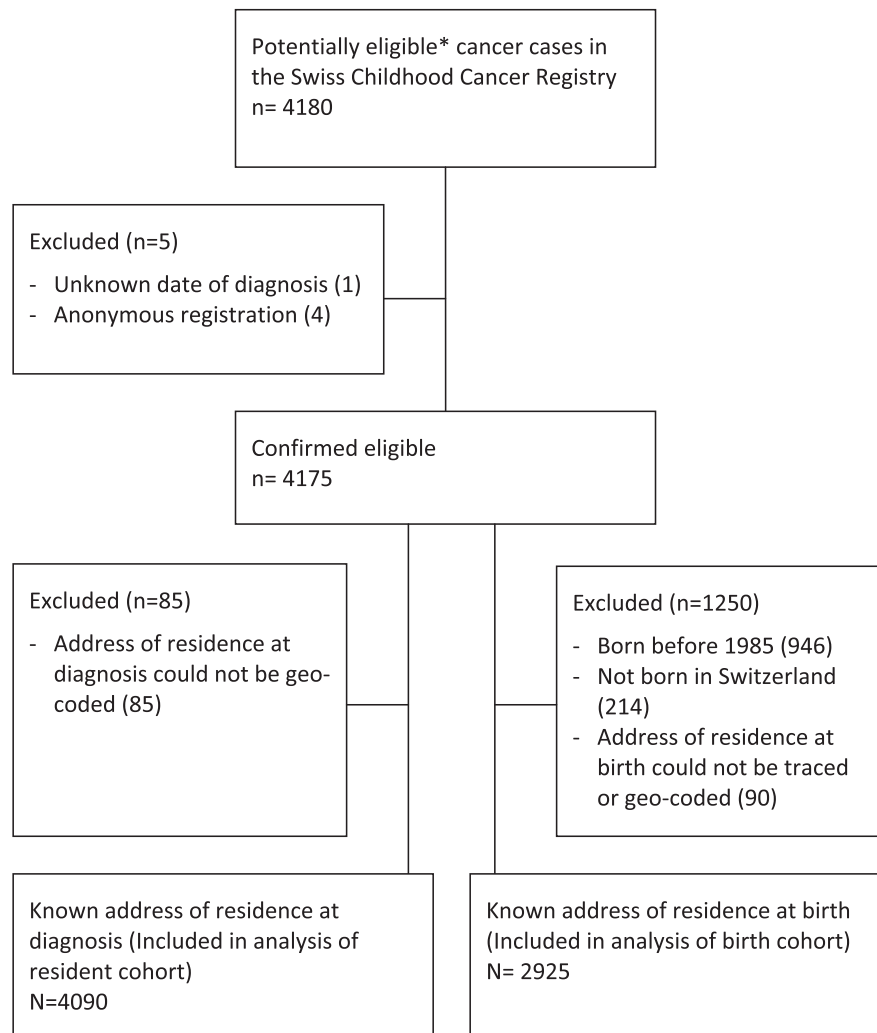
Incidence by distance to nuclear facilities

In the birth cohort, 8 and 12 children diagnosed with leukaemia at ages 0–4 and 0–15 years, respectively, and 18 and 31 children diagnosed with any cancer lived <5 km from a NPP at birth (Table 2,

Box 1 Description of sensitivity analyses and additional analyses

Analysis	Description	Background and rationale
Sensitivity analyses		
1	Account for airborne emissions by redefining the exposure as living in a zone around a NPP that is equivalent in area to a circle with 5 km radius, but extends to a distance proportional to the average duration of slow winds (<3 m/s) in a given direction. ^{a,b}	Stronger associations in this analysis compared with the main analysis would support a causal effect of airborne emissions from NPPs (radionuclides or other). Downwind concentrations of pollutants are inversely related to wind speed. ³⁴ We therefore defined an exposure zone based on the direction of slow winds.
2	Exclude children living >50 km from a NPP.	Concentration of emissions from NPPs decrease rapidly with distance and will be virtually zero at distances >50 km. Regional differences in incidence rates in children living >50 km from NPPs, which are not related to emissions from NPPs, could have introduced bias.
3	Exclude calendar years 1985–90 and 2009.	Registration in the SCCR was less complete in 1985–90 and 2009.
4	Exclude children born abroad or before 1985 from the resident cohort.	Differences between the results for the birth and resident cohort might be due to the fact that the birth cohort includes only children born in Switzerland ≥ 1985 , whereas the resident cohort also includes children born <1985 and children who were born abroad. This sensitivity analysis eliminates the difference in the two study populations.
5	Use an alternative method to calculate person-years. ^a	The main analysis calculates person-years for a particular age group and calendar year based on the number of children of the same age in the two census years. The alternative method uses the number of children belonging to the same cohort in the census years instead.
6	Recalculate distance to nearest NPP by excluding each NPP in turn.	To investigate whether results were influenced by the characteristics of a particular NPP. Beznau I & II and Leibstadt are excluded together because of their proximity to each other.
7	Stratify the analysis by calendar period (1985–94 and 1995–2009).	All NPPs were in operation 1985–2009. Differences in results between the earlier and later periods might indicate confounding by unknown time-varying factors, or changes in emissions over time.
8	Include only children who remained in the same community since birth. ^b	Families with children at greater risk of developing cancer may have preferentially relocated closer or further away from NPPs as the children grew older. This could have affected results when using addresses at diagnosis, compared with addresses at birth.
Additional analyses		
9	Use $1/(\text{distance in km})$ as a continuous exposure variable.	To avoid the loss of information caused by categorising the exposure variable. According to an atmospheric dispersion model, air concentrations of radionuclides are approximately proportional to $(\text{distance in km})^{-1.4}$. ³⁴ We chose $(\text{distance in km})^{-1}$ for comparability with previous studies. ^{4,5}
10	Perform a direct comparison of distances to nearest NPPs between cases and the population at risk using two-sample <i>t</i> -tests and the Mann–Whitney U-test. We used addresses at birth of cases born in 1988–92 and 1998–2002 and addresses of infants in the 1990 and 2000 census populations. Only distances <50 km were included. ^b	This analysis avoids computation of person-years; rather it uses the directly observed distances of the population at risk in the census years. It also avoids categorising the exposure variable as in analysis (9), but unlike (9), no assumptions about the relationship between distance to NPPs and cancer incidence are made.

^aFurther details given in Supplementary Appendix 1, available as Supplementary Data at *IJE* online.^bFurther details given in Supplementary Appendix 2, available as Supplementary Data at *IJE* online.



* Eligibility: all children with a diagnosis classified in the International Classification of Childhood Cancer (third edition) or a Langerhans cell histiocytosis, diagnosed between 1st Jan 1985 and 31st Dec 2009 at age 0–15 years and resident in Switzerland at diagnosis.

Figure 2 Flow chart of selection of children with childhood cancer

and Figure 3). IRRs (95% CI) for leukaemia diagnosed in 0–4 and 0–15 year olds, comparing children in this inner circle with children living >15 km away, were 1.20 (0.60–2.41) and 1.05 (0.60–1.86), respectively. The corresponding IRRs for any cancer were 0.97 (0.61–1.54) and 0.89 (0.63–1.27). In the 5–10 km zone, IRRs tended to be <1 for all outcomes; in the 10–15 km zone they were close to 1 for 0–15 year olds and slightly >1 in 0–4 year olds. A similar variation of IRRs around 1 was observed for distance to any nuclear facility and for distance to sites of NPPs that were planned but never built (Table 2 and Figure 3). In all analyses, the 95% CIs included 1 and there was little evidence of a dose–response relationship (*P*-value from test for linear trend ≥ 0.3).

In the resident cohort, 11 and 20 children in age groups 0–4 and 0–15 years, respectively, lived within

5 km of a NPP when diagnosed with leukaemia, and 23 and 50 children, respectively, were diagnosed with any cancer (Table 3 and Figure 4). Compared with children living >15 km away, IRRs for children in the 0–5 km zone were >1 for leukaemia in 0–4 and 0–15 year olds: 1.41 (95% CI 0.78–2.55) and 1.24 (95% CI 0.80–1.94). Corresponding IRR for any cancer were 1.11 (95% CI 0.74–1.67) and 1.03 (0.78–1.36). For the 5–10 km zone, IRRs were <1 for both outcomes and age groups. In the analyses including any nuclear facility, IRRs were again >1 in the 5 km zone for leukaemia in 0–4 and 0–15 year olds (Table 3 and Figure 4). IRRs by distance to planned but not built NPPs were close to 1 (Table 3, and Figure 4). Again, in all analyses the 95% CIs included 1 and *P*-values for a linear trend across distance categories were ≥ 0.1 .

Table 1 Characteristics of childhood cancer cases included in birth and resident cohorts

	Birth cohort <i>n</i> (%)			Resident cohort <i>n</i> (%)		
	Included		Excluded 0–15 years	Included		Excluded 0–15 years
	0–4 years	0–15 years		0–4 years	0–15 years	
Diagnosis (ICCC3)²⁰	1618 (100.0)	2925 (100.0)	1250 (100.0)	1830 (100.0)	4090 (100.0)	85 (100.0)
I Leukaemias, myeloproliferative diseases and myelodysplastic diseases	573 (35.4)	953 (32.6)	413 (33.0)	680 (37.2)	1345 (32.9)	21 (24.7)
II Lymphomas and reticuloendothelial neoplasms	72 (4.4)	303 (10.4)	242 (19.4)	88 (4.8)	530 (13.0)	15 (17.6)
III CNS and miscellaneous intracranial and intraspinal neoplasms	252 (15.6)	594 (20.3)	228 (18.2)	273 (14.9)	796 (19.5)	26 (30.6)
IV Neuroblastoma and other peripheral nervous cell tumours	227 (14.0)	242 (8.3)	33 (2.6)	245 (13.4)	274 (6.7)	1 (1.2)
V Retinoblastoma	88 (5.4)	92 (3.1)	10 (0.8)	93 (5.1)	101 (2.5)	1 (1.2)
VI Renal tumours	143 (8.8)	182 (6.2)	52 (4.2)	166 (9.1)	232 (5.7)	2 (2.4)
VII Hepatic tumours	28 (1.7)	37 (1.3)	7 (0.6)	28 (1.5)	43 (1.1)	1 (1.2)
VIII Malignant bone tumours	11 (0.7)	115 (3.9)	83 (6.6)	13 (0.7)	195 (4.8)	3 (3.5)
IX Soft tissue and other extra-osseous sarcomas	96 (5.9)	184 (6.3)	77 (6.2)	106 (5.8)	255 (6.2)	6 (7.1)
X Germ cell tumours, trophoblastic tumours and neoplasms of gonads	38 (2.3)	68 (2.3)	41 (3.3)	40 (2.2)	104 (2.5)	5 (5.9)
XI and XII Other malignant epithelial neoplasms and malignant melanomas or unspecified malignant neoplasms	13 (0.8)	44 (1.5)	27 (2.2)	14 (0.8)	70 (1.7)	1 (1.2)
Langerhans cell histiocytosis	77 (4.8)	111 (3.8)	37 (3.0)	84 (4.6)	145 (3.5)	3 (3.5)
Gender						
Male	894 (55.3)	1621 (55.4)	711 (56.9)	1007 (55.0)	2278 (55.7)	54 (63.5)
Female	724 (44.7)	1304 (44.6)	539 (43.1)	823 (45.0)	1812 (44.3)	31 (36.5)
Median age at diagnosis in years (interquartile range)	2.2 (1.0–3.4)	4.3 (2.0–8.6)	10.4 (6.0–13.5)	2.3 (1.2–3.5)	5.8 (2.6–11.2)	7.6 (3.5–12.3)

ICCC3, International Classification of Childhood Cancer, third edition; CNS, central nervous system.

Table 2 Incidence of childhood cancer in birth cohort according to distance to nuclear power plant, any nuclear facility and NPPs that were planned but never built

Age 0–4 years					Age 0–15 years			
Cases	PY at risk in 100 years	IR per 100 000 PY	IRR (95% CI) ^a		Cases	PY at risk in 100 years	IR per 100 000 PY	IRR (95% CI) ^a
Distance to nearest NPP (km)								
Leukaemias								
0–5	8	1000	8.00	1.20 (0.60–2.41)	12	2548	4.71	1.05 (0.60–1.86)
5–10	12	3011	3.99	0.60 (0.34–1.06)	25	7631	3.28	0.73 (0.49–1.09)
10–15	31	4194	7.39	1.10 (0.77–1.58)	47	10487	4.48	0.99 (0.74–1.33)
>15	522	77 375	6.75	1	869	190 509	4.56	1
All cancers								
0–5	18	1000	17.99	0.97 (0.61–1.54)	31	2548	12.17	0.89 (0.63–1.27)
5–10	43	3011	14.28	0.77 (0.57–1.04)	89	7631	11.66	0.85 (0.69–1.05)
10–15	92	4194	21.94	1.17 (0.95–1.44)	156	10 487	14.88	1.08 (0.92–1.27)
>15	1465	77 375	18.93	1	2649	190 509	13.91	1
Distance to nearest nuclear facility (NPP, research, or storage) (km)								
Leukaemias								
0–5	39	5034	7.75	1.15 (0.83–1.59)	65	12 184	5.34	1.16 (0.90–1.50)
5–10	32	6013	5.32	0.79 (0.55–1.13)	57	14 624	3.90	0.85 (0.65–1.12)
10–15	41	5858	7.00	1.05 (0.76–1.44)	62	14 547	4.26	0.95 (0.73–1.22)
>15	461	68 674	6.71	1	769	169 821	4.53	1
All cancers								
0–5	94	5034	18.67	0.98 (0.80–1.21)	180	12 184	14.77	1.07 (0.92–1.24)
5–10	103	6013	17.13	0.90 (0.74–1.11)	200	14 624	13.68	0.99 (0.86–1.14)
10–15	130	5858	22.19	1.18 (0.99–1.42)	217	14 547	14.92	1.09 (0.95–1.25)
>15	1291	68 674	18.80	1	2328	169 821	13.71	1
Distance to nearest planned NPP (km)								
Leukaemias								
0–5	5	1387	3.60	0.54 (0.22–1.31)	13	3443	3.78	0.85 (0.49–1.47)
5–10	53	6627	8.00	1.20 (0.90–1.60)	79	16 102	4.91	1.09 (0.87–1.38)
10–15	55	8126	6.77	1.01 (0.77–1.34)	97	19 557	4.96	1.10 (0.89–1.36)
>15	460	69 439	6.62	1	764	172 073	4.44	1
All cancers								
0–5	26	1387	18.74	0.98 (0.67–1.45)	48	3443	13.94	1.00 (0.75–1.33)
5–10	127	6627	19.16	1.00 (0.83–1.20)	223	16 102	13.85	0.98 (0.86–1.13)
10–15	145	8126	17.84	0.93 (0.78–1.10)	260	19 557	13.30	0.94 (0.83–1.07)
>15	1320	69 439	19.01	1	2394	172 073	13.91	1

^aAdjusted for sex, age and calendar year at diagnosis.

PY, person-year; IR, incidence rate; IRR, incidence rate ratio; NPP, nuclear power plant.

Adjustment for confounders and sensitivity analyses

Results were closely similar when adjusting, one at a time, for potential confounders (Figures E1–E30 of Supplementary Appendix 2, available as Supplementary Data at *IJE* online). As shown in Figure 5, the results from the sensitivity analyses were closely similar to the main analysis (detailed results are

shown in Figures E31–E48 of Supplementary Appendix 2, available as Supplementary Data at *IJE* online). In the analyses using 1/(distance in km), estimated IRRs were close to 1 for the birth cohort and >1 for the resident cohort, with 95% CIs including 1 (Figure E49 in Supplementary Appendix 2, available as Supplementary Data at *IJE* online). The results of the direct comparison of distances to nearest NPP

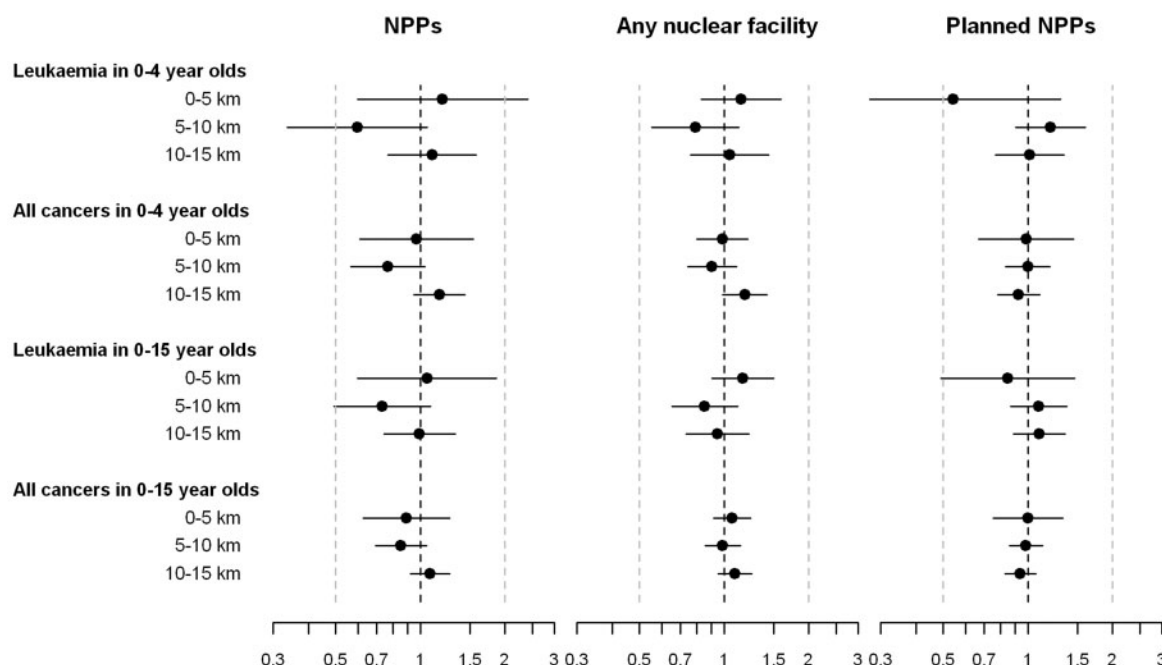


Figure 3 Results for birth cohort. Incidence rate ratios adjusted for sex, age and year at diagnosis and 95% CIs comparing children living in the inner 5 km, 5–10 km and 10–15 km zones with children outside the 15 km zone. Results for nuclear power plants (NPPs); any nuclear facility including NPPs, research and storage facilities; and sites of planned but not built NPPs are shown

between childhood cancer cases and the population at risk are shown in Table E2 in Supplementary Appendix 2, available as Supplementary Data at *IJE* online. Among infants living <50 km from a NPP, cases born in 1988–92 and diagnosed with leukaemia at 0–4 years lived on average 28.70 km (SD 11.53 km) from a NPP at birth compared with 27.62 km (11.85 km) for the population at risk in 1990 (P -value Mann–Whitney test: 0.38). Results were similar for other outcomes. Differences were found in 2000 for any cancer in 0–4 years, with cases living slightly closer to NPPs ($P=0.01$). However, histograms show that cases were mainly overrepresented at intermediate rather than small distances from NPPs (Figures E50–51 in Supplementary Appendix 2, available as Supplementary Data at *IJE* online).

Discussion

This nationwide census-based cohort study found little evidence of an association between residence near NPPs and the risk of leukaemia or any childhood cancer, either for residence at birth or at diagnosis. In particular, there was no evidence for a dose-response over distance categories, results were not changed by adjustment for confounders and remained robust in numerous sensitivity analyses designed to evaluate potential biases related to the study population, modelling of person-years or definition of exposure. However, due to the small number of cases, statistical

power was limited and we cannot exclude a moderately increased or reduced incidence in the 0–5 km zone, particularly for leukaemia in children aged 0–4 years.

Methodological considerations

A major strength of this study is the nationwide cohort approach, leaving little room for selection bias. Only two other studies used a cohort approach^{14,24} and one of them did not study the 5 km zone around NPPs.¹⁴ The German case-control study was criticized for control selection bias, with controls selected retrospectively from community records and community response rates varying by distance to NPPs.^{4,5} By using census data to compute person-years and a national cancer registry to obtain incident cases, we avoided participation bias. There was no evidence that variation in the completeness of the SCCR biased our results: findings were similar when we adjusted for distance to the nearest paediatric cancer centre, excluded children living further than 50 km from any NPP or excluded calendar years with poorer registration coverage. As all Swiss NPPs were built in populated regions near large paediatric cancer centres (Bern, Aarau, Zurich) any bias would likely have strengthened rather than attenuated associations.

Our main analysis was based on residence at birth: humans are particularly sensitive to ionizing radiation during intrauterine development and infancy;¹⁵ there

Table 3 Incidence of childhood cancer in resident cohort according to distance to nuclear power plant, any nuclear facility and NPPs that were planned but never built

Age 0–4 years					Age 0–15 years			
Cases	PY at risk in 100 years	IR per 100 000 PY	IRR (95% CI) ^a		Cases	PY at risk in 100 years	IR per 100 000 PY	IRR (95% CI) ^a
Distance to nearest NPP (km)								
Leukaemias								
0–5	11	1094	10.06	1.41 (0.78–2.55)	20	3784	5.29	1.24 (0.80–1.94)
5–10	20	3297	6.07	0.85 (0.54–1.32)	35	11 255	3.11	0.73 (0.52–1.02)
10–15	34	4542	7.49	1.05 (0.74–1.48)	66	15 039	4.39	1.02 (0.80–1.31)
>15	615	85 579	7.19	1	1224	282 721	4.33	1
All cancers								
0–5	23	1094	21.03	1.11 (0.74–1.67)	50	3784	13.21	1.03 (0.78–1.36)
5–10	57	3297	17.29	0.91 (0.70–1.18)	133	11 255	11.82	0.92 (0.77–1.10)
10–15	105	4542	23.12	1.21 (0.99–1.47)	222	15 039	14.76	1.14 (0.99–1.30)
>15	1645	85 579	19.22	1	3685	282 721	13.03	1
Distance to nearest nuclear facility (NPP, research, or storage) (km)								
Leukaemias								
0–5	47	5389	8.72	1.21 (0.90–1.62)	90	17 244	5.22	1.19 (0.96–1.48)
5–10	42	6687	6.28	0.86 (0.63–1.18)	74	22 367	3.31	0.76 (0.60–0.97)
10–15	39	6480	6.02	0.83 (0.60–1.15)	91	21 545	4.22	0.98 (0.79–1.21)
>15	552	75 955	7.27	1	1090	251 643	4.33	1
All cancers								
0–5	104	5389	19.30	0.99 (0.81–1.21)	254	17 244	14.73	1.13 (0.99–1.28)
5–10	125	6687	18.69	0.96 (0.80–1.16)	286	22 367	12.79	0.99 (0.87–1.11)
10–15	139	6480	21.45	1.12 (0.94–1.33)	312	21 545	14.48	1.13 (1.00–1.26)
>15	1462	75 955	19.25	1	3238	251 643	12.87	1
Distance to nearest planned NPP (km)								
Leukaemias								
0–5	12	1563	7.68	1.07 (0.60–1.89)	24	5222	4.60	1.09 (0.72–1.63)
5–10	58	7270	7.98	1.11 (0.85–1.46)	112	23 555	4.76	1.11 (0.92–1.35)
10–15	60	8950	6.70	0.93 (0.71–1.22)	130	29 322	4.43	1.04 (0.87–1.24)
>15	550	76 728	7.17	1	1079	254 700	4.24	1
All cancers								
0–5	35	1563	22.39	1.15 (0.82–1.61)	70	5222	13.40	1.03 (0.81–1.31)
5–10	141	7270	19.39	0.99 (0.83–1.18)	323	23 555	13.71	1.04 (0.93–1.16)
10–15	159	8950	17.77	0.90 (0.77–1.06)	370	29 322	12.62	0.95 (0.86–1.06)
>15	1495	76 728	19.48	1	3327	254 700	13.06	1

^aAdjusted for sex, age and calendar year at diagnosis.

PY, person-year; IR, incidence rate; IRR, incidence rate ratio; NPP, nuclear power plant.

is a latency between exposure and development of cancer;¹⁵ and young families tend to move. Therefore, studies based on residence at diagnosis might suffer from exposure misclassification, and address at birth will be a better proxy for the place of residence during pregnancy. Whereas most previous studies were ecological using community mid-points to determine the distance to the nearest NPP, our

study used precise (<50 m in most cases) residential locations, thus allowing the calculation of exact distances. Finally, we adjusted for many potential confounders, including background ionizing radiation,²⁶ non-ionizing radiation,²⁷ traffic-related carcinogens²⁸ and proxies for population mixing.²⁹

The main weakness of our study is the relatively small sample size, particularly of 0–4 year olds living

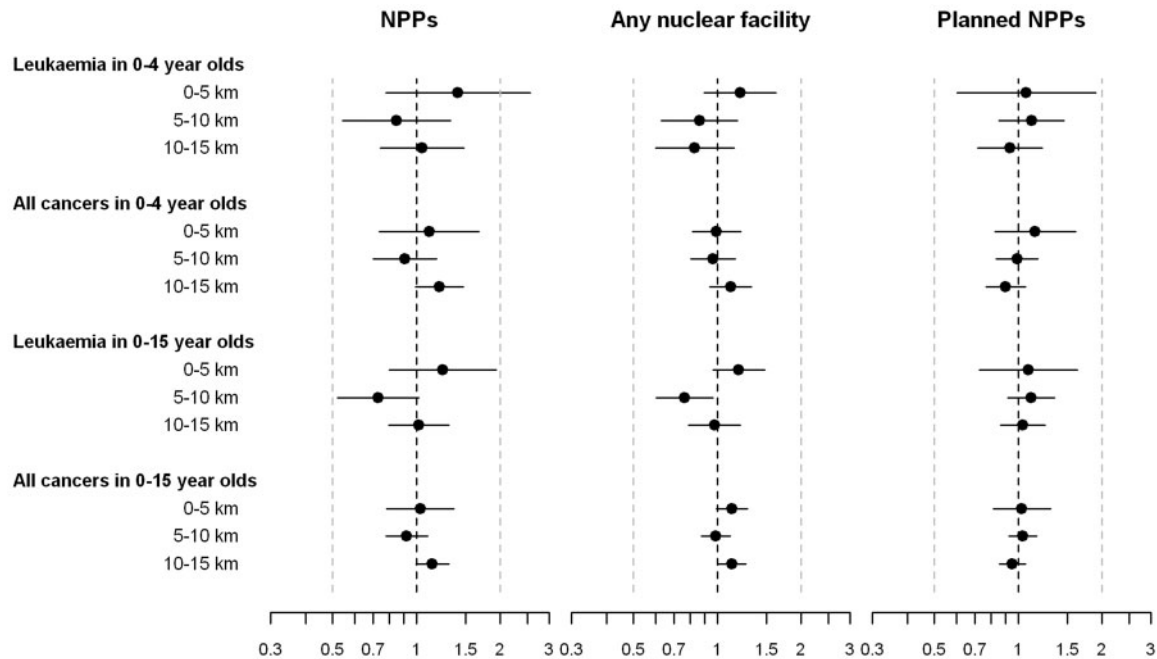


Figure 4 Results for resident cohort. Incidence rate ratios adjusted for sex, age and year at diagnosis and 95% CIs comparing children living in the inner 5 km, 5–10 km and 10–15 km zones with children outside the 15 km zone. Results for nuclear power plants (NPPs); any nuclear facility including NPPs, research and storage facilities; and sites of planned but not built NPPs are shown

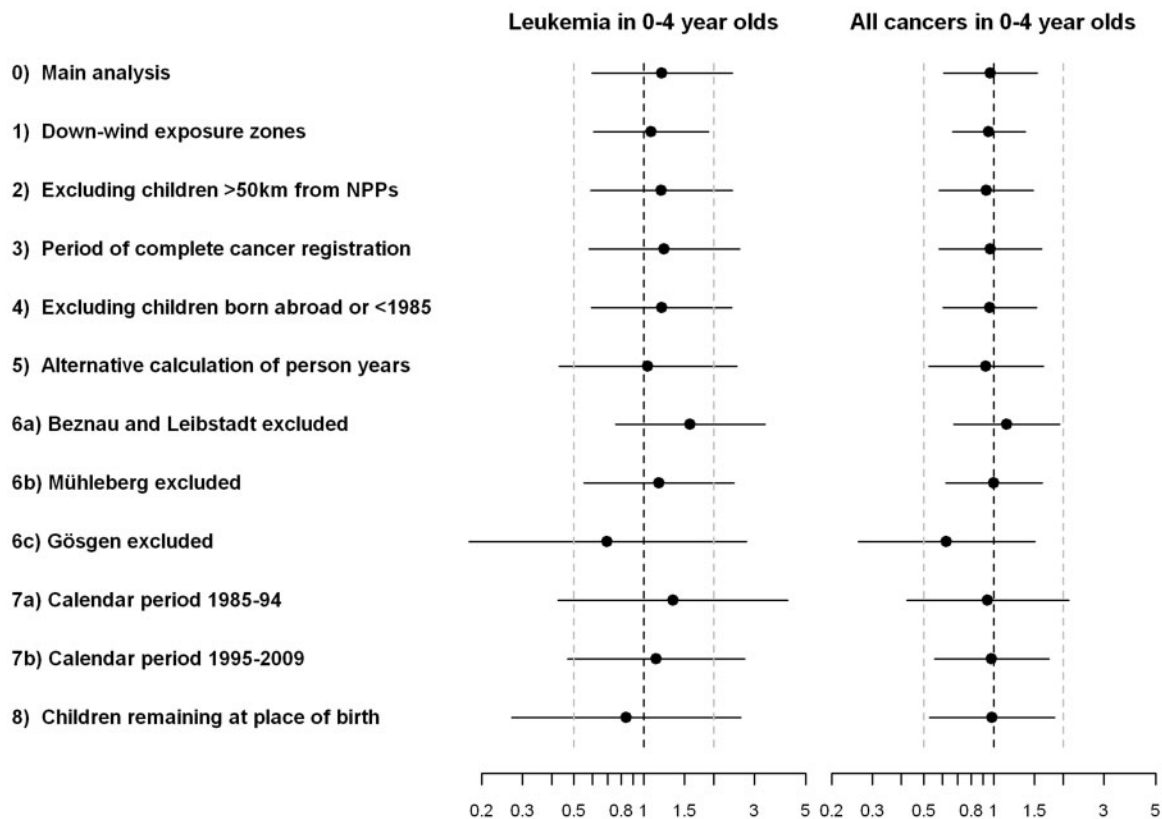


Figure 5 Comparison of results of main and sensitivity analyses. Incidence rate ratios adjusted for sex, age and year at diagnosis and 95% CIs comparing children living <5 km with children living >15 km from a nuclear power plant. Results are shown for the birth cohort and are adjusted for sex, age and year at diagnosis. Analyses numbered as in Box 1

close to NPPs, resulting in large CIs around estimated IRRs. Second, we could not adjust for some potential individual or family level confounders, such as health behaviours, diet, infections, medical radiation or medications. However, with the exception of high dose radiation treatment, these exposures are all weak risk factors (if at all) and thus unlikely to be strong confounders.²² Another methodological limitation of our and other studies^{14,24} was the need to compute person-years from census data. We accounted for non-linear population fluctuations at the aggregate level, but internal migration was only accounted for by linear inter-/extrapolation of person-years between and around census years. Finally, the birth cohort did not include cases who had emigrated before diagnosis. However, data from the Swiss National Cohort show that only 2% (4%) of <1 year olds in the 1990 census had emigrated in the first 4 (15) years of life, making emigration an unlikely source of bias.

Our results in context with the literature

Most previous analyses, summarized in recent reviews,^{13,30,31} were ecological, using routine data to calculate standardized mortality or incidence ratios. Studies of local clusters near single NPPs have been performed for 198 different sites in 10 countries. Among these, only three clear clusters emerged (Seascale near Sellafield, Dounreay, Kruemmel), two relating to nuclear processing rather than power generating stations. A meta-analysis of 136 single nuclear facilities concluded that there was evidence of an excess leukaemia risk near NPPs.³⁰ However, the methodology of this study has been criticized.³² A total of 25 studies from eight countries analysed leukaemia risk in the vicinity of several NPPs.³¹ Overall, these show no consistent evidence for an increased risk of childhood leukaemia near NPPs. Few, however, have specifically investigated leukaemia in under-fives living close (<5 km) to NPPs.^{4,9,13,24,33,34} Among these, the German case-control study, the only other study using exact distances, found elevated ORs for leukaemia (OR 2.19, lower one-sided confidence limit 1.51) and all cancers (OR 1.61, lower one-sided confidence limit 1.26).^{4,5} The Committee on Medical Aspects of Radiation in the Environment (COMARE) recently analysed the data for children aged 0–4 years when diagnosed with leukaemia or non-Hodgkin lymphoma 1969–2004.¹³ The analysis was based on electoral wards and postcode zones near 13 NPPs in the UK and showed no evidence for an increased risk in the 5-km perimeter: the relative risk was 1.01 (compared with the national average), with relatively narrow 95% CI (0.70–1.47). Interestingly, the analysis of six possible locations for NPPs, where no installation was constructed, showed an increased risk: 1.72 (95% CI 1.12–2.52), for reasons that are not understood.¹³ A similar

approach in France found no evidence for increased IRRs in the 5 km zone (IRR 0.96, 95% CI 0.31–2.24).³¹

Population-attributable risks and potential causes

Assuming the association is causal and the point estimate from the analysis of the birth cohort (IRR 1.20) reflects the true underlying effect for leukaemia, 1.3 (0.2%) of the 573 leukaemia cases observed during the 25-year study period in 0–4 year olds would be attributable to living <5 km from a NPP. If we assume that the upper confidence limit (IRR 2.41) reflects the true underlying effect, 4.7 cases (0.8%) would be attributable to living <5 km from a NPP. Repeating the analysis for all cancers, using the upper confidence limit (IRR 1.54), 6.3 cases (0.4% of 1618 cases) would be attributable to living near a NPP. Exposure to radioactivity set free by the nuclear facilities is unlikely to explain an excess in cancer risk in their vicinity. The NPPs are responsible for <1/500 of the total radiation received yearly by people living near NPPs; the main sources are natural radiation and medical examinations.¹⁶ Other hypotheses that could explain a link between leukaemia and NPPs include paternal exposure to radiation before the child's conception³⁵ or an infectious agent linked to population mixing near NPP sites.³¹

Conclusions

In summary, this nationwide cohort study, adjusting for confounders and using exact distances from residence at birth and diagnosis to the nearest NPPs, found little evidence for an association between the risk of childhood cancer and living near NPPs.

Supplementary Data

Supplementary Data are available at *IJE* online.

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Conflict of interest: None declared.

KEY MESSAGES

- This large-scale study examined the association between childhood cancer and residence near nuclear power plants at birth and at diagnosis.
- The study found little evidence of an association, either for residence at birth or residence at diagnosis, but the number of exposed cases was small and confidence intervals wide.
- Results remained consistent after adjustment for potential confounders and in a number of sensitivity analyses.
- A major strength of this study was the nationwide cohort approach, leaving little room for selection bias.

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